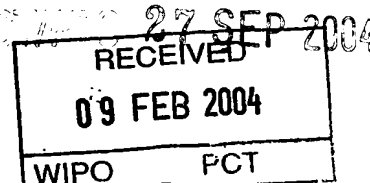




**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
(PCT Article 36 and Rule 70)



Applicant's or agent's file reference <b>AXP/PG4790</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/EP 03/03338</b>	International filing date ( <i>day/month/year</i> ) <b>27.03.2003</b>	Priority date ( <i>day/month/year</i> ) <b>28.03.2002</b>
International Patent Classification (IPC) or both national classification and IPC <b>C07D265/30</b>		
Applicant <b>GLAXO GROUP LIMITED</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  <b>30.09.2003</b>	Date of completion of this report  <b>05.02.2004</b>
Name and mailing address of the international preliminary examining authority:   <b>European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840</b>	Authorized Officer  <b>Hass, C</b>  Tel phon No. +49 30 25901-340  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/03338**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-20 as originally filed

**Claims, Numbers**

1-12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/03338**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 4 (with regard to industrial applicability)  
because:
  - ☒ the said international application, or the said claims Nos. 4 relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.
- ☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-8, 10-20
	No: Claims	9
Inventive step (IS)	Yes: Claims	1-8, 10-20
	No: Claims	9
Industrial applicability (IA)	Yes: Claims	1-3, 5-20
	No: Claims	

2. Citations and explanations

**see separate sheet**

**R Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claim 4 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Cited documents**

- D1: WO 98 56771 A (SCHERING AG) 17 December 1998 (1998-12-17) cited in the application
- D2: SARTORI E ET AL: 'SYNTHESIS AND ACTIVITIES OF NET ARYLSULFONAMIDO THROMBOXANE A2 RECEPTOR ANTAGONISTS' EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 28, no. 7/8, 1993, pages 625-632, XP000396678 ISSN: 0223-5234 cited in the application
- D3: WO 95 31431 A (NISSHIN FLOUR MILLING CO; KIKUCHI HARUHIKO (JP); SATOH HIROAKI (JP) 23 November 1995 (1995-11-23)
- D4: EP-A-0 243 959 (DAINIPPON PHARMACEUTICAL CO) 4 November 1987 (1987-11-04)
- D5: WO 95 31442 A (NISSHIN FLOUR MILLING CO; KIKUCHI HARUHIKO (JP); SATOH HIROAKI (JP) 23 November 1995 (1995-11-23)

**2. Novelty**

**2.1 The subject-matter of claim 9 is not novel** in view of D2, page 631, left-hand column, line 17 ("methyl 3-aminomethyl benzoate").

**2.2 The subject-matter of claims 1-8 and 10-12 is novel** with regard to D1-D5: The D1 compounds have no morpholine ring.

The D3 compounds similar to those of claims 1, 6 and 7 have no "free" urea group (D3, pages 28 and 35). The compound disclosed on page 41, line 5 of D3 does not have a ring on the "left-hand side" of the molecule.

The compound disclosed in D4, page 43, example 24 has an amide group as linking group.

The compound disclosed in D5, page 40, lines 6-10, is different from the compounds claimed in claims 11 and 12 at least because it has no A-corresponding group.

### **3. Inventive step**

**3.1** According to the description, the problem underlying the present application is to provide further compounds which are useful as pharmaceuticals, especially for the treatment of inflammation.

**3.2** For the subject-matter of claim 1, D1 is the closest prior art since it also discloses compounds which have anti-inflammatory activity. However, the D1 compounds are piperazine derivatives, and they do not have a urea group. The present compound of claim 1 thus could not be deduced from D1. Therefore it can be said that the problem as defined above has been solved in a non-obvious way. For the subject-matter of product claim 1, process claim 2, pharmaceutical claims 3 to 5 and of claims 6 to 8 and 10 to 12, which are directed to intermediates (claim 9 is not novel, see above), inventive step can be acknowledged.

### **4. Industrial applicability**

**4.1** The subject-matter of claims 1-3 and 5-12 is industrially applicable.

**4.2** For the assessment of the present claim 4 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.